REVIEW ARTICLE



Stephen F. Mason—structural chemist and historian of science—a centenary remembrance

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Abstract

Stephen F. Mason (1923–2007) was a polymath. He applied a variety of spectroscopic and computational techniques to investigate molecular properties. His best-known results appeared in connection with chirality. He was a pioneer in advocating the importance of chiral separation for pharmaceuticals even before the thalidomide tragedy. Another pioneering contribution was his work on biomolecular homochirality and the recognition of the electroweak origin of biomolecular handedness. He published important books spanning the range from the history of science through the chemical history of the elements to the origin of the universe and life. Our remembrance focuses on his views on some turning points in the history of science and, especially, in the history of chemistry.

Keywords Stephen F. Mason · History of science · Chirality · Biomolecular homochirality · Chiral discrimination

"Scientists could and should advertise to the public that technical solutions are accessible, where not already available, for most environmental problems, and that the real problem is social, the economic and political factors involved in the funding and implementation of scientifically-based solutions".

Stephen F. Mason

Stephen F. Mason (1923–2007, Figs. 1 and 2) was one of the rare polymath scientists in the second half of the twentieth century. He was both a practical bench researcher and a science historian. He differed from anybody else, who has combined these two interests, in that he was first a science historian and only then a research physical/structural chemist. He was not yet 30 years old when he wrote his most successful book, *The history of the sciences: main currents of scientific thought* [1]. Subsequently, he moved to chemical research, was especially successful in his studies of molecular chirality, and published groundbreaking treatises. His broad vision and knowledge led to the production of further books that discussed such fundamental problems as the origin of the universe and the origin of life. In 2000, I recorded

⊠ Istvan Hargittai stuceditor@gmail.com a long conversation with him [2] and the narrative of this remembrance is based primarily on this conversation. In our meeting, he spoke about his road to science and this is augmented with information from Roger Grinter's biographical memoir [3], an excellent survey for getting to know Stephen Mason, his time, and his work.

Stephen F. Mason was born in the village of Anstey, Leicestershire, England. His father, Leonard Stephen Mason, ran a garage, and his mother, Chrissie Harriette Mason (née Finney–this is where Mason's middle name came from), ran their home. The parents eventually separated. Mason lived at home until he was 18 years old. He liked to play with discarded motor parts, built experiments with discarded car batteries, and was interested in the lives of plants that grew in their garden. He read books from the family library; one of them was about spectra.

He attended the village school for primary education, 1928–1933, and, on scholarship, the Wyggeston Grammar School for Boys in Leicester, 1933–1941. He had good science masters in biology, physics, and chemistry. The distinguished British crystallographer, Alan L. Mackay (b. 1926), noted that in the 1930s, "... the school teaching was often excellent and the teachers had first class degrees in science and mathematics. During and after the Depression first-class graduates were glad to get a job in teaching, and this produced the immediate post-war generations of scientists" [4].

Mason was awarded an open scholarship at Wadham College, Oxford University, where he studied chemistry and

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Fig. 1 Stephen F. Mason, 2000, in Cambridge, UK (photograph by and courtesy of Magdolna Hargittai)

biochemistry. His university experience included exposure to poets and artists, and learning about politics, economy, and philosophy. He made friends, participated in debates, and stood up for science in opposition to religion. He attended lectures of famous chemists, such as N. V. Sidgwick and the future Nobel laureate C. N. Hinshelwood. A former Sidgwick pupil, Dalziel L. Hammick (1887–1966), was Mason's tutor. Hammick was known not only for good chemistry but also for his independent thinking.

Mason took up research on antimalarial drugs for the Army Medical Corps and then the Medical Research Council. The goal was to find a practical method of detecting whether Italian prisoners of war were taking their antimalarial pills. Many of the prisoners of war were employed as farm laborers in the environs of Oxford and they passed on their antimalarial pills to local girls as contraceptives. A method was found by which fluorescence showed the presence of the antimalarial metabolites in the prisoners' urine. Mason then continued to study the physical chemistry of various factors that might be used to enhance the relative efficacy of different antimalarial drugs. He was awarded a B.A. with First Class Honors (1945), and an M.A. and D.Phil. (1947). In 1967, he was awarded a D.Sc. degree by Oxford University, a largely honorary distinction rather than being a prerequisite for higher positions as it is in many European countries.

The antimalarial research was fairly routine, and he had ample time to study the history of chemistry. As a result, Mason wrote an essay for a Prize Fellowship in 1947. The assessor of the essay was F. Sherwood Taylor (1897–1956), the curator of the Oxford Museum of the History of Science. Taylor was impressed by Mason's treatise and invited him to be a demonstrator at the Museum. His duties included giving lectures of general interest on the history of science. He held the post, in conjunction with a tutorship in chemistry at Wadham College, until 1953. Toward the end of his appointment, he completed his first book, *A history of the sciences* [1].

At that point, the Warden of Wadham College, Sir C. Maurice Bowra (1898–1971), urged Mason to return to chemical research. The job situation did not promise real possibilities in the history of science. Mason followed the advice, and this is how his reverse career move happened in contrast to many others. The usual sequence is that scientists enter the studies of science history following a research career elsewhere in science. For Mason, the change was not hard to make as he missed the practical work of a chemistry laboratory, and the quest for new substances, mechanisms, and theories. He felt that having learned about science history made him a better researcher and broadened his world view.

In 1953, he was appointed to be an associate of the Department of Medical Chemistry, Australian National University (ANU). The physical plant of the department was being built in Canberra, and for the time being, it was actually located in the Wellcome Institute in London. Adrien Albert (1907-1989) was the head of the department and Mason's work involved the investigation of the physical chemistry of the mode of action of pharmaceuticals. There was a connection with Mason's earlier work, because Albert was an international authority on biologically active acridines, which were related to antimalarial substances. In 1955, Mason's laboratory, while still being part of ANU, was moved to the Biochemistry Department of University College London (UCL). This was another opening for interactions with interesting associates both at this department and the Chemistry Department of UCL where a great deal of innovative research was being carried out in physical chemistry and in particular, spectroscopy. Mason could build on his Oxford experience where he used to apply infrared spectroscopy as well as ultraviolet spectroscopy in his work.

In 1955, Mason attended the first of the Summer Schools in Theoretical Chemistry, organized by Charles Coulson (1910–1974), then Rouse-Ball Professor of Mathematical Physics at Oxford. The School introduced young chemists to the molecular orbital (MO) theory. This tool further broadened Mason's perspective for the interpretation of molecular



spectra and the study of molecular structures and reaction mechanisms. When Mason was an undergraduate, quantum mechanics was not taught to chemistry students. Coulson's summer schools introduced some 35 to 60 chemistry graduate students, postdoctoral fellows, and university lecturers to the subject each year, from 1955 to 1973. Coulson's lectures were crystal clear, and his communication went beyond the power of his words. One had to work hard at the problems he set, as part of the course, to really understand what he had said. Mason treasured the memory of his interactions with Coulson and called him the evangelical teacher of quantum chemistry. Mason was an atheist whereas religion was an authentic part of Coulson's life who used to deliver sermons on Sundays. Mason remembered him as a kindly man of singular probity and dedication over a range of scientific and social concerns whose criticisms were invariably constructive. Around 1970, Mason nominated Coulson for the Nobel Prize in Chemistry, citing his contributions to molecular orbital theory. The nomination was not successful. Some other supporters of Coulson told Mason that Coulson, as a matter of principle, would not engage in the kind of lobbying in Stockholm that seemed to accompany successful Nobel awards.

When Mason's Australian research fellowship in London ended in 1956, he did not move to Australia. Rather, he took up a lectureship in chemistry at the new University of Exeter. The 8 years he spent at Exeter was professionally the most important period in his research career. He started doing spectroscopy of chiral molecules in connection with a general problem. It was the use of synthetic racemic compounds in homochiral biochemical applications, medical and agricultural. Emil Fischer (1852–1919) had shown that the chemistry of living organisms is homochiral, involving mainly one of the two optical isomers of the organic compounds. They were characterized by Louis Pasteur in 1848 as handed (chiral, dissymmetric), with non-superposable mirror-image structural forms (enantiomers), and with equal and opposite rotations of the plane of linearly polarized light in solution. Optical isomerism led Le Bel and van 't Hoff in 1874 to recognize the four valencies of the carbon atom being directed to the vertices of a tetrahedron.

The expectations of isomerism in chains of chiral carbon atoms were confirmed and used as a guide by Fischer in his investigations of the sugar series and then the aminoacid series in natural biochemical products. These chemical relationships led Fischer to conclude that virtually all structural and functional proteins were composed of L-amino acids, while the carbohydrates were composed of D-sugars. Here, L and D refer to a conventional absolute configuration of four different groups around a chiral carbon atom. In 1951, it was shown by X-ray crystallography that Fischer had made the correct choice in his convention for absolute stereochemical configuration.

Around 1950, most synthetic chiral pharmaceutical drugs were racemic mixtures of two enantiomers, although it was known to pharmacologists that the separated enantiomers had different biological activities. Mason suggested to the head of Imperial Chemical Industries (ICI) Pharmaceuticals that racemic pharmaceuticals should be resolved and only the enantiomer with the selective activity be used medically. The industry leader responded that the expense of the resolution would be ruinous. This was before the thalidomide tragedy after which new legislation required the testing of the individual enantiomers of racemic pharmaceuticals. Thus, for example, one enantiomer of warfarin retards blood-clotting more effectively than the other, by a factor of five in humans, and by a factor of nine in rats.

At Exeter, Mason and his colleagues constructed a CD spectrophotometer for the visible and quartz ultraviolet (UV) region, and later on in London (at King's College), CD instruments for the vacuum-UV and the IR region. Their goal was to determine the absolute stereochemical configuration of an enantiomer from a comparison of the experimental CD with that calculated from model structures. At the same time, they investigated new methods for resolving racemic mixtures into their individual enantiomers, and the stereoselective interactions between chiral systems. Mason covered these studies in his 1982 book Molecular optical activity and the chiral discriminations [5]. Among others, he writes about the possible origin of the built-in handedness in the organic world. His teaching was then extended in his 1991 book Chemical evolution: Origins of the elements, molecules and living systems [6].

In the 1960s, there was a rapid expansion of the UK university system and Mason received attractive offers to chair newly established chemistry departments. He accepted the one from the University of East Anglia at Norwich, and stayed there between 1964 and 1970. He continued his studies of optical activity and his chirality works brought him international recognition. He did not find though sufficient attraction in building up a new school and when the opportunity arose, he moved to a professorship at King's College in London. This turned out to be his longest assignment and stayed there until his retirement in 1988. He had a small group, always about six associate so he could work with them directly.

The Japanese Reiko Kuroda was one of them who had been attracted by a postdoctoral position with Mason. Kuroda, as a woman PhD, could have hardly hoped for any position in science in Japan, so this move saved her career. Mason needed someone to determine absolute configuration by X-ray crystallography. Kuroda had known of Mason from the literature and was happy that a world-renowned expert would let her work in his group. The atmosphere in Mason's group was very friendly. She arrived with hardly any knowledge of English, and was helped to feel herself comfortable. Many years later the situation had changed in Japan, she returned home, and became the first female full professor at Tokyo University. She never left the area of studies related to chirality [7].

The Nobel Prize for Physics in 1979 was awarded to Sheldon L. Glashow, Abdus Salam, and Steven Weinberg for the unification of electromagnetism with the weak nuclear force, including the discovery of the chiral electroweak interaction. This development enhanced the interest in biological chirality. The choice of specifically L-amino acids and D-sugars, rather than their enantiomers, in the homochiral biochemistry of the organic world used to be regarded as a matter of chance. Specific mechanisms, such as the photochemical effects of cosmic circularly polarized radiation, might generate either enantiomer of the amino acids and of the sugars. The electroweak interaction prescribes a determinate helicity, which is left-handed for electrons (anti-parallel spin and momentum vectors). By 1983, Mason and his associates incorporated the electroweak interaction as a perturbation into their ab initio MO calculations. They found that the L-amino acids are inherently more stable, although only by a minuscule amount, than the corresponding D-enantiomers. One of his associates, the postdoctoral research fellow George Tranter, found that the D-sugars have a similar stability increment over their L-enantiomer counterparts.

When Mason retired, he and his (second) wife, Joan Banus (1923–2004), also a research chemist, moved to Cambridge. By then, their three sons had grown up so they were the two of them, and they continued their research. He returned to the history of science and she was active in the movement for the improvement of the situation of women in science. My wife and I visited them in 2000 in their home and Mason and I recorded a long conversation, which we finalized for publication through extended correspondence [2].

As we talked about the history of science, I felt a nostalgic undercurrent in his opinion about the importance of this subject. When he was a student, each topic was usually introduced by an outline of its brief history. Chemical reviews contained critical histories with sidetracks and dead ends of selected research lines. As time went by, he observed the ever shrinking space allotted to such history introductions giving more attention to "state-of-the-art" and covering at most the developments of only the past few years. He stressed the benefits of gaining a broader perspective, which fostered an interdisciplinary approach to solving problems and better utilization of past experience. Instead, the researchers have been increasingly preoccupied with current and specialized concerns.

Below, I communicate two extended excerpts from our conversation. These excerpts may be interesting even for those who had read Mason's monograph of the history of science, because in his retirement, he was working on updating it. His death prevented him from completing the revision, so his updating, perhaps except what appeared in our published conversation, has never been printed.

What are the highlights of the history of chemistry for you?

The two main aspects of the history of science that primarily concern me are the ways in which we have attained a progressively enlarged understanding of the natural world, and, through this development, how the sciences have been used to tackle social and technical problems.

The modern period of history begins around the time of the Protestant Reformation during the early sixteenth century, when it was perceived that what passed for the sciences needed reformation to bring about "the relief of man's estate," as Francis Bacon (1561–1626, Fig. 3) put it. The "Luther of medicine," Paracelsus (1493-1541) tried to transform the wealth-seeking metallurgical alchemy of earlier times into a new iatrochemistry¹ with more humanitarian medical aims, based on mineral as well as herbal remedies, and he secured a substantial following over the next century or so. The ancient notion that all substances were composed of a relatively passive body and an active spirit lived on, and the distillation and bottling of spirits containing the potent essences of the substrates flourished on an industrial scale. The iatrochemist van Helmont (1597–1644), under house arrest in Brussels by the Spanish Inquisition for some 20 years, discovered that some spirits could not be condensed and bottled, yet they turned out to be powerful and individual derivatives of their substrates. He termed the non-condensible spirits "gases," opening up the era of pneumatic chemistry.

The Unitarian minister Joseph Priestley (1733–1804, Fig. 4) made spectacular contributions to pneumatic chemistry, isolating and characterizing more than a dozen different gases by their chemical reactions. Priestley was already concerned with the pollution of the atmosphere, during the early phase of the industrial revolution in Britain, and devised a method of measuring the "goodness of the air," from the changes in a volume of air after reaction with nitric oxide and condensation of the product in water. Subsequently, he was delighted to discover that green plants in sunlight restore the "goodness of the air" by producing the vital gas, oxygen. Priestley was a radical in politics and religion. His support for aspects of the French Revolution led to the torching of his manse, library, and laboratory in Birmingham by a mob of "patriots" led by some of the county gentry, and he felt obliged to emigrate to the newly independent USA in 1794. Yet Priestley remained enmeshed in the ancient alchemical body-spirit model at a time when it was being superseded during the Chemical Revolution led by Lavoisier (1743–1794) and other French chemists, who interpreted combustion as oxidation. Combustion, for Priestley, led to



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Fig. 3 Statue of Sir Francis Bacon by William Theed, Jr., 1869, in one of the ground-story niches on the right-hand side of Burlington House, 6 Burlington Gardens, W1, London. Photograph by Magdolna and Istvan Hargittai, reproduced from [8]

the *calx*, the "dead body," of the substrate, with the release of the spirituous *phlogiston*, which he came to identify with electricity. Electrochemistry was only just starting up in 1800, and another century elapsed before G. N. Lewis convincingly identified oxidation with electron-loss and reduction with electron-gain.

The Chemical Revolution, as it was termed in France, or the "new French chemistry" as it was referred to elsewhere, centered on the long-known "augmentation of the *calx*," the

¹ Iatrochemists tended to interpret physiology in terms of chemistry.



Fig. 4 Statue of Joseph Priestley by Gilbert Bayes, 1915, above the entrance, 30 Russell Square, WC1, London. Photograph by Magdolna and Istvan Hargittai, reproduced from [8]

increase in weight of a substrate on combustion. The discovery of oxygen gas by Priestley enabled Lavoisier to ascribe the weight increase to the uptake of oxygen from the air, and the energy changes to the release of the imponderable matter of heat, *caloric*.

The nomenclature reform of the French chemists was of fundamental importance, replacing the old body-spirit terminology, with new terms, based on oxygen. The *calx* was now termed the oxide, and the "spirit of vitriol" became sulfuric acid. The assumption that oxygen was the "acid generator," as its name implied, was flawed, but the systematic nomenclature based on the increase of acidity with increase of oxygen content lived on, e.g., the acidic component of the sulfides, sulfites, and sulfates. The definition of a chemical element as "the latest term whereat chemical analysis has arrived" was not really new, but now led to the proliferation of new inorganic compounds, hundreds from different elements taken two at a time from Lavoisier's



Fig. 5 Statue of John Dalton by Francis Chantrey, 1838, at the Manchester City Hall. Photograph by Magdolna and Istvan Hargittai, reproduced from [8]

list, thousands if taken three at a time. Some had remarkably useful properties, such as the new bleaching reagents, which saved England, during the vast expansion of the textile industry, from becoming a huge bleaching field, relying on sunlight and the oxygen of the atmosphere for a bleaching effect.

The theoretical rationalizations made in 1800-1820 of the enormous body of chemical data now accumulating were largely ignored until the 1860s. The theory of John Dalton (1766–1844, Fig. 5) postulated that the chemical elements fell into distinct species, with the identical atoms of one species differing in relative weight and combining propensities from the atoms of other species. His law of multiple proportions (1804) indicated that the weight ratios of two elements forming two or more compounds were simple integers, quantizing atomic combining capacities, as in the oxides of nitrogen, N₂O, NO, and NO₂. A similar simple integer ratio held for the volumes of combining gases, as Gay-Lussac (1778–1850) found in 1808: one volume of hydrogen and one volume of chlorine at the same temperature and pressure combine to give two volumes of hydrogen chloride. Hence, the gaseous elements must be composed of diatomic molecules, deduced Avogadro (1776-1856) in 1811, for each unit of hydrogen gas, as also each unit of gaseous chlorine, must split to produce two units of hydrogen chloride. Not necessarily so, argued Ampère (1775–1836) in 1814, for Gay-Lussac's law shows only that there is an even number of atoms in the molecule of an element. Molecules are the basic building blocks of three-dimensional crystals, and molecules should be three-dimensional too, composed at a minimum of four atoms in a tetrahedral array. The average practicing inorganic chemist of the time maintained that none of the theoreticians could be taken seriously. In any event simple tables of equivalents, the combining weights of the elements relative to oxygen, or another standard element, sufficed for most practical purposes.

Such an approach led to confusion in the new field of organic chemistry emerging during the 1830s. So few elements entered the composition of organic compounds, basically carbon and hydrogen, then oxygen and nitrogen, and other elements only in more exotic cases. Gaseous acetylene and liquid benzene both analyzed to [CH]_n, but a value for *n* could be obtained only from the molecular weights of the two molecules. Perceptive French organic chemists in the 1840s began to argue for a revival of Avogadro's hypothesis, according to which the molecular weight of a volatile organic substance, relative to the unit weight of a hydrogen atom, is given by twice the vapor density of the substance, relative to that of molecular hydrogen. German and British chemists joined the discussions in the 1850s, and the matter was largely solved after deliberations at a comprehensive international conference, the first of its kind, held at Karlsruhe in 1860, with 140 chemists attending. Here, Cannizzaro (1826-1910) showed how a systematic application of the hypothesis of his fellow Italian, Avogadro, to series of related molecules gave consistent sets of atomic and molecular weights, and the atomic combining numbers, their valencies.

Mendeleev (1834–1907, Fig. 6) returned to Russia where he worked out his Periodic Classification of the 67 chemical elements then known, with gaps for missing elements, whose properties he predicted in detail (1869). A primary organizer of the conference, Kekulé (1829-1896), worked out a testable flatland stereochemistry of aromatic molecules in 1865, based on the hexagonal ring structure for benzene. The structure rationalized the known features of aromatic chemistry, and its detailed expectations served as a guide for further explorations of the field, including the synthetic coal-tar dyes. Aliphatic organic chemistry was less well rationalized during the 1860s, for there remained the mysterious problem of optical isomers, two substances apparently identical in all chemical and physical properties, except for their equal and opposite rotation of the plane of polarized light in solution.



Fig. 6 Statue of Dmitry I. Mendeleev by Matvei G. Manizer and Elena A. Yanson-Manizer, 1953, in one of the two entrance lobbies of the Ceremonial Hall in the central building of Lomonosov Moscow State University, Vorobyovy Hills, Moscow. Photograph by Magdolna and Istvan Hargittai, reproduced from [9]

Pasteur in 1848 had provided a general morphological answer. A pair of optical isomers in solution must have overall dissymmetric forms, non-superposable mirrorimage shapes, like their corresponding crystal forms in the solid state, whatever their internal structure might be. Pasteur then moved on, as a founder of microbiology, to study the diseases of wines and beers, of silkworms, dogs, cattle, and humankind, surveying with a critical eye chemist who claimed to synthesize optically active molecules without the use of a chiral physical force which, he believed to the end of his days, was active throughout the cosmos. So it was left to Le Bel (1847-1930) and to van 't Hoff (1852-1911) to work out the internal structure of optical isomers, showing independently in 1874 that two non-superposable mirror-image forms are generated if four different atoms or groups in a tetrahedral array are bonded to a central carbon atom. The expectations of the tetrahedral model for the orientation of the four valencies

of carbon were worked out and confirmed in detail, especially and spectacularly by Fischer for the sugar series (1884–1908) and then the natural amino acids and the peptides (1908–1919).

Fischer showed that Pasteur's chiral force of nature was not required to account for the homochirality of biomolecules, the prevalence of the D-series of sugars, and the L-series of amino acids among natural products. The reactions of symmetric, non-chiral reagents adding a new potentially chiral carbon atom to an enantiomer did not give the two expected products (diastereomers, containing two or more chiral carbon atoms) in equal quantity. Such reactions were stereoselective, and one of the diastereomeric products appeared in often substantial excess. With enzyme catalysis, such reactions became stereospecific, affording a single diastereomeric product. Fischer concluded that there is no need to postulate the continuous operation of a chiral force in biosynthesis, as Pasteur had supposed, "once a molecule is asymmetric, its extension proceeds also in an asymmetric sense." Given a primordial enantiomer, biochemical evolution necessarily gave rise to chiral homogeneity among the variety of natural products, through Fischer's "key and lock" mechanism, the survival of the best stereochemical fits in biomolecular reactions, ensuring an efficient and economic biosynthesis and metabolic turnover.

The chirality of the primal enantiomer appeared to be wholly a matter of chance, for left- and right-handed chiral forms of the classical forces and energy fields seemed to be equally abundant, and sum to zero over a time and space average, such as those involved in natural helical motions or circularly polarized radiation. This viewpoint was enshrined in Wigner's (1927) principle of the conservation of parity, which implied that an organic world based on the D-amino acids and L-sugars would be wholly equivalent to the actual biomolecular world characterized by Fischer, based on the enantiomeric series. The weak interaction responsible for radioactive beta-decay was found to violate the principle of the conservation of parity in 1956. Subsequently, the weak interaction was unified with electromagnetism, and the massive boson carriers of the integrated electroweak interaction were detected at CERN in 1983. It appeared that the neutral component of the electroweak interaction might provide an attenuated form of Pasteur's universal chiral force of nature, adequate enough to account for the minor prebiotic enantiomeric excess from which Fischer's "key and lock" biomolecular evolution started. A residual effect would be an inherent, if miniscule, greater stability of the L-amino acids and the D-sugars relative to the corresponding enantiomeric series, as was found to be the case in subsequent quantum mechanical estimations incorporating the neutral electroweak interaction.

Reading Lucretius today, it is strikingly modern but we may be projecting our knowledge onto what we read. Did he and the other Greek and Roman philosophers have an impact on the emergence of modern science?

Part of the Renaissance and Reformation of the early modern period lay in the revival of ancient philosophies, beliefs, and styles, eclipsed during the middle ages. The Humanists revived the "pure" Latin vocabulary and style of Cicero and his contemporaries, to replace the "barbaric" medieval Latin with its Arabic and Germanic intrusions. The Protestant Reformers set out to revive the early authentic Christianity of the Church Fathers, as they interpreted it in individualistic and divergent ways. Philosophers looked to the precursors of Thomism, dominant in the thinking of the Roman Church since the thirteenth century, back to a "purified" Aristotelianism, freed from theological accretions, or to the Neoplatonism of the early centuries AD and other beliefs of early Imperial Rome associated with the official cult of the Divine Unconquerable Sun, such as Hermeticism. Philosophers of nature went back further to the Pre-Socratic Greeks, particularly the atomists, revived already by Lucretius (c.95–55 BC) in the pre-imperial Republican Rome.

Decartes (1596–1650), for example, revived the vortex cosmology of Anaxagoras (c.488–428 BC), who had been charged with impiety for his views, but saved by the intervention of Pericles, and Descartes withheld his mechanistic natural philosophy on hearing of the condemnation of Galileo in 1633. Descartes delayed full publication of his cosmology until he had worked out a theological buttressing for his views, but the censors were not satisfied, and the works of Descartes in 1663 were placed on the Roman Index of Prohibited Books (widely consulted by Protestant librarians for books to add to their libraries).

Copernicus (1473–1543) deleted a reference to the heliocentric cosmology of Aristarchus of Samos (c.310-230 BC), declared impious in antiquity, from the manuscript of his own book, published in 1543, On the Revolutions of the Heavenly Spheres, reviving and elaborating the suncentered astronomical system. The early use of the book was not problematic, for a Lutheran pastor, Osiander, who saw the book through the press in 1543, inserted an anonymous foreword declaring that the Copernican scheme was hypothetical, designed to save the astronomical appearances, not a physical cosmology, which it became in the hands of Kepler (1571-1630), the maverick Lutheran Imperial Mathematician to the Hapsburg Holy Roman Emperors. But it was the qualitative telescopic discoveries of Galileo (1564–1642) that gave the Copernican system a widespread plausibility, the observation around 1610 of mountains and apparently seas on the moon, of spots on the sun, the phases of Venus, and the four moons of Jupiter. Copernicanism then became a doctrine banned by the Roman Church (1616) "until corrected," and Galileo was condemned for his support of the doctrine in 1633.

Classical atomism was especially abhorred during the early centuries AD and the middle ages as "atheistic." In fact, Epicurus and Lucretius held that the gods were indifferent to the autonomous workings of nature and the activities of humankind, a view akin to that of the deism widespread during the eighteenth century, holding that, after the Creation, God left the machine of the universe and its creatures to run themselves automatically. Such views jeopardized the claims of the Roman emperors and their historical "ghosts" (as Hobbes put it in his Leviathan of 1651), the Popes of the Roman Church, to temporal power based on a privileged direct communication with their cosmic representative, first the Deus Sol Invictus and then the Christian God. Lucretius appears to have been copied and read surreptitiously during the medieval period. There are two ninth century copies of On the Nature of Things by Lucretius in the Leiden University Library. The title page of one copy had been torn out, and the name of the author had been erased and replaced by a pseudonym on the title page of the other.

Atomism was revived during the sixteenth and seventeenth centuries in the disguised form of corpuscularianism, a natural philosophy of particles in motion. Heat increased the motions of the particles of bodies, according to Francis Bacon. All of space was filled with very fine particles, Descartes supposed, and their motions set up the vortices that swept the earth and the planets in circular orbits around the sun, or of the sun and planets around the earth from the point of view of an observer beyond the sphere of fixed stars, he added, in a concession to the ban of the Roman Church on the Copernican scheme. Boyle supposed that corpuscles were polyatomic conglomerates, exchanging parts in chemical reactions. The corpuscles of the air might be stationary springs, with mutual repulsion as they approached one another. This mechanism would explain the inverse proportionality between pressure and volume (Boyle's law), as would a mechanism involving the air particles in motion, where the frequency of collisions between the particles and the walls of the container, and thus the pressure, would increase as the volume of the container was diminished.

Classical atomism was gradually made more theologically acceptable during the seventeenth century, through the postulate that God originally created atomic matter and set the atoms into such motions as produced the natural world and its creatures according to providential design. Atomism had an appeal for the mentality of assertive individualism, developed by Renaissance writers and radical Reformers, and prominent among the leaders of the great geographical explorations and their mercantile backers. Intellectual supporters were moved to give their own individual interpretations of the Book of Nature and the Book of Holy Writ. Interpretations and assertions as to the content of the Book of Nature mostly could be checked empirically, but rather less so in the case of those referring to Scripture, and a consequent progressive secularization led to the Deists of the eighteenth century, who recapitulated much of the theological stance of the atomists of antiquity.

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